

## **REMARKS**

The Office Action mailed October 1, 2002, has been received and its contents carefully noted. Claims 1-19 were pending and claims 1-19 were rejected. By this amendment, claim 4 has been amended and claims 20-26 have been added. Support may be found in the specification and claims as originally filed. Specific support for claims 20 and 21 may be found on page 7 of the specification. Specific support for claim 22 may be found on page 10 and support for claims 23-26 may be found on page 11 of the specification. No statutory new matter has been added. Reconsideration is respectfully requested.

### **Claim Objections**

The Examiner objected to claim 4 because the recitation "water or water" appears to be a typographical error.

Applicants respectfully submit that claim 4 as amended addresses the typographical error. Therefore, the objection should properly be withdrawn.

### **Rejection under 35 U.S.C. §112, first paragraph**

The Examiner rejected claims 3, 13-16, 18 and 19 under 35 U.S.C. 112, first paragraph, as being nonenabled. Specifically, the Examiner deemed that the specification and prior art do not enable the method of stopping the loss of hair

or the method of using prostaglandins EP-2 and EP-4 receptor agonists.

Applicants respectfully submit that the specification clearly provides an enabling disclosure such that a person skilled in the art would be able to stop the loss of hair by using the compositions according to the invention as claimed. Several working examples and methods of stopping the loss of hair are disclosed in the specification. Lotions for preventing hair loss are provided in Examples 1 and 4 on pages 13 and 15. The lotion may be applied daily at an amount of 10 ml to the scalp for 2 to 3 months. Shampoos that prevent hair loss are provided in Example 2 on page 13. The composition of shampoo and method to stop loss of hair are disclosed. The shampoo may be used daily at an amount of 15 grams per head of hair, with an exposure time of about one minute, over a period of 4 months. Gels for preventing hair loss are provided in Example 3 on page 15. The composition of gel and method to stop loss of hair are disclosed. The gel may be applied twice a day (morning and evening) at an amount of 25 grams to the entire scalp via massaging into the scalp for 3 months.

Applicants submit that each of these Examples enables the present invention as claimed. As provided in these Examples, the methods and compositions show a marked slowing down in the daily loss of hairs. These observations prove the

efficacy of the claimed methods. Moreover, use of compositions according to the invention is disclosed (for example, shampoo in Example 2, page 13 containing prostaglandin EP-3 receptor antagonist and prostaglandin EP-2/EP-4 receptor agonist) leading to an appreciable slowing down in the daily hair loss.

Applicants respectfully submit that the criteria for determining whether an agent is a "prostaglandin EP-2 receptor agonist" or a "prostaglandin EP-4 receptor agonist" is known in the art. See for example, Narumiya (1999) Physiological Reviews 79(4):1193-1226. Narumiya discloses EP receptor antagonists and agonists and methods for determining their activity. See Figure 7, p. 1203, and p. 1204, table 1. Therefore, conventional methods for screening compounds for being EP antagonists or agonists is known in the art. Screening compounds having a given activity using methods known in the art is not undue experimentation.

Therefore, the invention as claimed is fully enabled and the rejection under 35 U.S.C. 112, first paragraph, should properly be withdrawn.

#### **Rejection under 35 U.S.C. §112, second paragraph**

The Examiner rejected claims 13, 14 and 19 under 35 U.S.C. 112, second paragraph, as being indefinite. Specifically, the Examiner deemed that claims 13, 14, and 19 lack active, positive steps that delimit how the use is actually practiced.

Applicants respectfully submit that the claims as amended obviate the rejection. Therefore, the rejection under 35 U.S.C. 112, second paragraph, should properly be withdrawn.

#### **Rejection under 35 U.S.C. § 102(b)**

The Examiner rejected claims 1, 2, 13-16 and 19 under 35 U.S.C. 102(b) as being anticipated by Katsu et al. (CAPLUS abstract data 1987:55617, JP 61218510). Specifically, the Examiner deemed the "claimed method of 'attenuating, reducing, and stopping the loss of keratin materials' is within the scope of the prior art which uses the same active compound in promoting hair growth, which would result in overall reduction of loss of hair".

Applicants respectfully submit that Katsu et al. do not teach the use of the same active compound and for the same purpose. Specifically, Katsu et al. teach the use of an EP-3 agonist, PGE1, to promote hair growth. The present invention as claimed is directed to compositions comprising EP-3 antagonists

for use in methods for preventing hair loss. Hair growth and hair loss occur by different biological mechanisms. Thus, promoting hair growth may not necessarily prevent hair loss and preventing hair loss will not necessarily promote hair growth. EP-3 antagonists do not encompass PGE1 and PGI2, which are EP-3 agonists.

On page 6 of the specification, an antagonist is a substance that binds a receptor, but does not induce the usual biological response of the native ligand for the receptor. In the present invention, the prostaglandin EP-3 receptor antagonist binds the same receptor as prostaglandin E, but induces a different result, prevents hair loss rather than promotes hair growth. Furthermore, the structural features of prostaglandin EP-3 receptor antagonist and prostaglandin E are different.

Therefore, Katsu et al. do not anticipate the present invention as claimed, and the rejection under 35 U.S.C. 102(b) should properly be withdrawn.

The Examiner also rejected claims 1, 13-16 and 19 under 35 U.S.C. 102(b) as being anticipated by Hanson (U.S. Pat. No. 5,605,932). Specifically, the Examiner deemed that Hanson discloses a method of reducing hair loss by administering PGE1 and that for protection of hair follicles topical administration is especially suitable.

Applicants respectfully point out that PGE1 is an EP-3 receptor agonist rather than an antagonist. Hanson deals with the method of administration of prostaglandin type E to protect tissues from injury resulting from chemotherapeutic agents. In Example 2 of Hansen, the use of a prostaglandin E analog, i.e. misoprostol, is disclosed in order to protect hair follicles, hair loss, or alopecia, in cancer patients. Applicants respectfully submit that the prostaglandin EP-3 receptor antagonists and the PGE-type prostaglandins have different functions. Nowhere does Hansen disclose compositions comprising EP-3 receptor antagonists or methods of preventing or stopping hair loss comprising administering an EP-3 receptor antagonist. As Hansen does not disclose a composition containing prostaglandin EP-3 receptor antagonists, the present invention as claimed is novel.

Therefore, the rejection under 35 U.S.C. 102(b) should properly be withdrawn.

**Rejection under 35 U.S.C. § 103(a)**

The Examiner rejected claims 2-12, 17 and 18 under 35 U.S.C. 103(a) as being unpatentable over Hanson as applied to claims 13-16, and 19 and further in view of Bradbury et al. (U.S. Pat. No. 6,124,362) and Bernard et al. (U.S. Pat. No. 5,985,841). Specifically, the Examiner deemed that given the

specific teaching in Hanson that topical application of E-type prostaglandins are effective in treating hair loss, it would have been obvious to one of ordinary skill in the art to look for prior art such as Bradbury et al. for conventional topical formulations for hair loss with an expectation of successfully formulating a topical composition for alopecia. The Examiner deemed that a skilled artisan would have also adjusted the pH of the composition as taught by Bernard et al.

Applicants submit that Bradbury et al. discloses a method for regulating the growth and loss of hair via the use of compositions containing terpenes as active compounds to regulate growth and loss of hair. Bradbury et al. describes also cosmetically acceptable vehicles and ingredients including the optional use of prostaglandin agonists or antagonists as enhancers. Bradbury et al. do not list any type of prostaglandin agonists or antagonists or even list a few suitable examples of such. Nowhere do Bradbury et al. disclose the use of prostaglandin EP-3 receptor antagonists for preventing or stopping hair loss. Bradbury et al. do not alleviate the deficiencies of Hanson, i.e. teach or suggest the use of prostaglandin EP-3 receptor antagonists.

Applicants respectfully submit that Bernard et al. relates to a method for stimulating hair growth or retarding hair loss which comprises administering at least one

deoxyglucopyranoside in a range of pH acceptable for topical applications. Nowhere do Bernard et al. disclose or suggest the use of prostaglandin EP-3 receptor antagonists for preventing or stopping hair loss. Bernard et al. do not alleviate the deficiencies of Hanson, i.e. teach or suggest the use of prostaglandin EP-3 receptor antagonists.

As none of the cited prior art alone or in combination teach or suggest the use a prostaglandin EP-3 receptor antagonist to prevent or stop the loss of hair with a reasonable expectation of success, the present invention as claimed is nonobvious.

Therefore, the rejection under 35 U.S.C. 103(a) should properly be withdrawn.

#### **Double Patenting**

The Examiner provisionally rejected claims 1-19 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17-36 of copending Application No. 09/917,211.

Applicants respectfully submit that copending Application No. 09/917,211 discloses the use, in cosmetic preparations, of prostaglandin EP2 and/or EP4 receptor antagonists to attenuate, reduce or stop the growth of hair. Contrary to the purpose of Application No. 09/917,211, the



purpose of the present application is to attenuate, reduce or stop loss of hair.

To lead to these two different purposes, these two inventions implement two different means. Application No. 09/97,211 uses EP-2 and/or EP-4 receptor antagonists. The present application uses EP-3 antagonists. EP-2 and/or EP-4 receptor antagonists and prostaglandin EP-3 receptor antagonists act on different receptors to confer different biological responses.

Therefore, the presently claimed invention is patentably distinct from that of copending Application No. 09/917,211 and the obviousness double patenting rejection should properly be withdrawn.

The Examiner also provisionally rejected claims 1-19 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 09/917,274.

Applicants respectfully point out that the present invention as claimed is directed to preparations containing prostaglandin EP-3 receptor antagonists to attenuate, reduce or stop the loss of hair. Antagonists bind to receptors, but do not induce the usual biological response that is induced by the

receptors' native ligands. Copending Application No. 09/917,274 is directed to preparations of prostaglandin EP-3 receptor agonists to attenuate, reduce or stop the growth of hair. The agonists and antagonists of the two applications are different compounds having distinct biological properties with regard to the EP-3 receptor. Moreover, the purpose of the present invention is to attenuate, reduce or stop the loss of hair rather than attenuate, reduce or stop the growth of hair as claimed in copending Application No. 09/917,274.

Clearly, the technical problems solved by the two inventions, as well as the solutions, i.e. compositions, are different and patentably distinct. Therefore, an obviousness double patenting rejection of the present claims in view of the pending claims of copending Application No. 09/917,274 is improper and should be withdrawn.

#### **Request for Interview**

Applicants respectfully request either a telephonic or an in-person interview should there be any remaining issues.

#### **Extension of Time**

A Petition for an Extension of Time for three (3) months under 37 C.F.R. 1.136 and the appropriate fee are

submitted herewith to extend the time for responding to the Office Action to April 1, 2003.

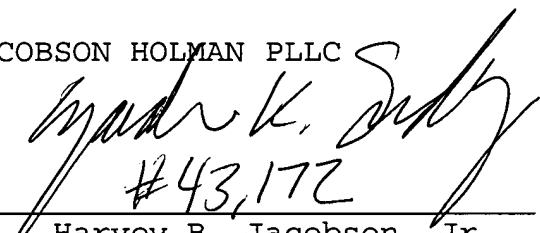
**Conclusion**

In view of the foregoing amendments and remarks, the Examiner is respectfully requested to reconsider and withdraw the rejection of the claims and to find this application to be in allowable condition.

Respectfully submitted,

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